REMARKS

Claims 1-6 and 10-12 are currently pending.

Claims 1 and 12 have been amended. Support for the amendment to claim 1 can be found at page 5, lines 1-35, page 6, lines 13-19, page 18, lines 1-20, and throughout the specification. Claim 12 has been amended to correct a typographical error: "stimulating" has been replaced with stimulate. No new matter has been added by the amendments.

The Office Action withdrew the rejection of claims 1-6 and 10-12 under 35 U.S.C. §112, second paragraph, for indefiniteness of the term "pluripotential cells" (see Office Action, page 2, paragraph 3).

Applicants respectfully request that the Attorney Docket No. for the above-referenced application be changed from "MER-011 CN/112917-144" to MER011CT.

Please reconsider the Application in light of the following remarks.

I. The Claims Meet the Requirements of 35 U.S.C. § 112, First Paragraph

Claim 1 and dependent claims 2-6 and 10-12 stand rejected under 35 U.S.C. § 112, first paragraph, for an alleged insufficient written description to show that Applicants were in possession of a "factor" in which to culture pluripotential cells which would cause them to express characteristics of DCs (Office Action, page 2).

Applicants traverse this ground of rejection but, for the sake of facilitating prosecution, claim 1 has been amended to specify that the factor is present in peripheral blood mononuclear cell conditioned medium, monocyte conditioned medium or macrophage conditioned medium. Page 27 of the specification describes assays which can be used to identify the factor. Applicants respectfully aver that one of ordinary skill in the art, at the time the invention was filed, would have been able to identify the factor following the guidance provided by the Application.

Further, Applicants respectfully disagree with the statement in the Office Action at page 3 that "it is clear that Applicant does not know (or did not know at the time of filing) the identity of the "factor" of the instant claims." Applicants aver that at the time the Application was filed, the Application clearly showed that Applicants possessed the maturation factor, particularly because the Application clearly teaches at page 27 how the ordinarily skilled artisan can identify

such a factor.

Also, Applicants respectfully disagree with the statement in the Office Action at page 3 that "Applicants conclude (but fail to demonstrate) that the stable, mature DCs generated by their method are made stable and mature by the factor of the instant claims. It could just as well be concluded that the DCs generated by the method of the claims are a result of the specific culture conditions or manipulations disclosed in the specification." Applicants have controlled for culture conditions and manipulations by culturing immature dendritic cells in the presence or absence of conditioned medium. Specifically, Figure 7 of the shows dendritic cells cultured from day 7 to 10 in RPMI/FCS without conditioned medium (panel A) or in the presence of RPMI plus conditioned medium (panel A'). As can be seen in Figure 7, dendritic cells cultured in the presence of conditioned medium have increased levels of CD83 and CD86, and decreased levels of CD115 (and are stable and mature), in contrast to dendritic cells cultured under the same conditions, but in the absence of conditioned medium. Thus, a factor present in conditioned medium, rather than some other culture condition or manipulation, generates the stable mature DCs.

In addition, Applicants respectfully disagree with the Office Action's characterization of the Steinman et al. Fundamental Immunology (1999) as questioning whether an actual factor exists. The Office action quotes Steinman as stating in this post-filing publication: "No one cytokine is responsible for DC maturation, and it is possible that a combination is required to induce the many different features of DCs." In contrast to the Office Action's characterization, this statement suggests that more than one cytokine may be responsible for DC maturation, rather than questioning whether a maturation factor exists. In this regard, page 5, lines 25-31 of the instant specification state: "The dendritic cell maturation factor may actually be one or more different substances, and may be provided by substances including, but not limited to PBMC conditioned media, maturation factors purified from the conditioned medium, and SACS (fixed Staphylococcus aureus Cowan 1 strain (Pansorbin))." Accordingly, Applicants respectfully aver that the claims meet the requirements of 35 U.S.C. §112, first paragraph, and therefore respectfully request that this rejection be reconsidered and withdrawn.

Claim 1 and dependent claims 2-6 and 10-12 were rejected under 35 USC § 112, first paragraph, for an alleged failure to provide written description to support dendritic cells with

decreased CD115 expression and decreased CD32 expression relative to the pluripotential cells. Specifically, the Office Action states that this is a new matter rejection, and that mature DCs are not compared to pluripotential cells.

Claim 1 has been amended to specify that an expression characteristic of *mature* dendritic cells (selected from the group consisting of increased CD83 expression, increased CD86 expression, decreased CD115 expression, and decreased CD32 expression) is compared to the expression in *immature dendritic* cells. Support for this amendment can be found at page 14, line 24, to page 15, line 2; at page 27, lines 10-22; page 55 lines 16 to 30. Accordingly, this rejection may be properly withdrawn.

Claim 1 and dependent claims 2-6 and 10-12 stand rejected under 35 USC § 112, first paragraph, for an alleged failure to provide a written description to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed. Specifically, the Office Action states: "[T]he specification discloses a method for producing stable mature dendritic cells having the potential of expressing either macrophage or dendritic cell characteristics, but not the broader method for producing [any type of] dendritic cells having the potential of expressing either macrophage or dendritic cell characteristics. Likewise, the specification discloses a method of producing mature DCs from immature DCs, said mature DCs comprising increased CD83 expression, increased CD86 expression, decreased CD115 expression, or decreased CD32 expression, but not the broader method of the claim." (Office Action, page 7).

Claim 1 has been amended to specify: contacting immature dendritic cells with a factor for a time sufficient for the immature dendritic cells to produce stable mature dendritic cells that express a characteristic of mature dendritic cells, wherein the characteristic is selected from the group consisting of increased CD83 expression, increased CD86 expression, decreased CD115 expression, and decreased CD32 expression relative to the immature dendritic cells. Accordingly, this rejection under 35 USC § 112, first paragraph may be properly withdrawn.

II. The Claims Meet the Requirements of 35 U.S.C. § 112, Second Paragraph.

Claim 1 and dependent claims 2-6 and 10-12 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to define the term "macrophage

characteristics in the specification.

Applicants respectfully traverse this rejection. Macrophage characteristics are disclosed in Figure 3 of the instant specification. Specifically, the legend to Figure 3 contrasts the morphology and phenotype of blood derived dendritic cells and macrophages. Dendritic cells are distinguishable from macrophages by their dendritic shapes, lack of CD14 expression, high p55 expression and perinuclear pattern (as opposed to a cytoplasmic pattern) of CD68 expression. In contrast, macrophages are rounded, CD14+, and express CD68 in a cytoplasmic pattern. Other characteristics of macrophages are disclosed in the specification, such as inability to induce a CTL response in CD8+ T cells (page 41, lines 13-17). Moreover, one of skill in the art at the time of filing could have readily distinguished macrophages from dendritic cells. See, for example, U.S. 5,994,126 (of record) column 28, which discloses a monoclonal antibody specific for macrophage F4/80 antigen. Accordingly, the rejection under 35 U.S.C. § 112, second paragraph may be properly withdrawn.

III. The Claims Meet the Requirements of 35 U.S.C. § 102.

Claim 1 and dependent claims 2-6 and 10-12 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No. 5,994,126, as evidenced by Kiertscher. According the to Office Action, the '126 patent teaches an *in vitro* method of producing DCs comprising culturing pluripotential cells comprising monocytes or mononuclear cells in GM-CSF and IL-4 to produce DCs with increased CD83, as evidenced by Kiertscher.

Claim 1 has been amended to specify a two step culture process that is not disclosed by the '126 patent. First, pluripotential cells are contacted with one or more cytokines for a time sufficient to produce an immature dendritic cell. Second, the immature dendritic cells are contacted with a factor for a time sufficient to produce stable mature dendritic cells, wherein the factor is present in peripheral blood mononuclear cell conditioned medium, monocyte conditioned medium or macrophage conditioned medium. In contrast, the '126 patent discloses contacting a pluripotential cell with a cytokine (such as GM-CSF) to produce dendritic cells (similar to the first step of amended claim 1), but does not disclose the second step of amended claim 1, which specifies culturing the immature dendritic cells produced by the first step with a factor (which can be found in peripheral blood mononuclear cell conditioned medium, monocyte conditioned medium or macrophage conditioned medium) to produce *stable mature* dendritic

cells specified by the amended claims. Thus, amended claim 1 and dependent claims 2-6 and 10-12 are not anticipated by the '126 patent. Accordingly, the rejection of claim 1 and dependent claims 2-6 and 10-12 under 35 U.S.C. §102(e) may be properly withdrawn.

Claim 1 and dependent claims 2-6 and 10-12 stand rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Romani et al., J. Exp. Med. 180: 83-93, 1994 ("Romani"), as evidenced by Caux et al. (Office Action at page 6).

Claim 1 has been amended to specify that immature dendritic cells are contacted with a factor for a time sufficient for the immature dendritic cells to produce stable mature dendritic cells that and express a characteristic of mature dendritic cells. Although the immature dendritic cells of Romani are treated similarly to a method described by the Application to generate immature dendritic cells (e.g., culturing PMBC in GM-CSF plus IL-4 for about one week), Romani does not disclose treating immature dendritic cells with a factor to produce stable mature dendritic cells, as is now specified in the amended claim 1.

Not surprisingly, given the differences in the method described by Romani as compared to the method of amended claim 1, the cells produced by Romani are immature dendritic cells that, once removed from the cytokines used to produce them, revert back to a pluripotential cell having characteristics similar to macrophages. It is the further maturation of these immature dendritic cells into stable mature dendritic cells that is one of the major features of the claims. Thus, claim 1 and dependent claims 2-6 and 10-12 are novel and unanticipated by Romani. Accordingly, the rejection under 35 U.S.C. §102(b) may be properly withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are in condition for allowance. However, if the Examiner believes that any further discussion of this communication would be helpful, she is encouraged to contact the undersigned by telephone.

A Petition for a three (3) month Extension of Time under 37 C.F.R. § 1.136(a) is filed concurrently herewith, which extends the response period from October 28, 2004 to January 28, 2005. The Petition authorizes the PTO to charge the three month extension fee of $510 to our Deposit Account No. 50-3187.

No other fees are believed to be due in connection with this communication. However,

please apply any additional charges, or credit any overpayment, to our Deposit Account No. 50-3187.

Respectfully submitted,

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Date: January 28, 2005

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